North America’s Premiere Mesothelioma Program at Princess Margaret Cancer Centre

Update Report
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INTRODUCTION

We are grateful for your remarkable support of Princess Margaret Cancer Centre’s Mesothelioma Program, the only one of its kind in North America. Our ultimate priority is to improve diagnosis and treatment for mesothelioma patients at The Princess Margaret, across the country and around the world. Our multi-disciplinary and highly accomplished mesothelioma team is on the front lines every day, ensuring patients receive the best possible care and support.

NORTH AMERICA’S PREMIER MESOTHELIOMA PROGRAM

Through your generosity, The Princess Margaret has become a global leader in treating mesothelioma, a form of cancer common among trade workers that originates in the lining of the lungs. A large majority (80%) of the close to 500 new cases diagnosed every year in Canada are caused by known exposure to asbestos in the workplace.

The Princess Margaret has created an advanced research facility and extensive infrastructure for the early detection, rapid assessment and treatment of mesothelioma. The Mesothelioma Program, led by Dr. Marc de Perrot, a leading thoracic surgeon in Canada, sees more patients with this disease than any other cancer centre in the country. In 2013 alone, The Princess Margaret handled almost half of all mesothelioma cases in Canada. Every year, more and more patients are being referred to Dr. de Perrot. If the demand continues to grow, the clinic may need to expand.

The Princess Margaret is the only Canadian site to be funded by the U.S National Cancer Institute to conduct early Phase I/II clinical trials of first-in-human studies of new cancer drugs. Currently, four such studies are open specifically for mesothelioma.

“Despite the fact that the use of asbestos was banned in most Western countries in the 1970s and early 1980s, the incidence of multiple malignant mesothelioma is still rapidly rising, with almost 500 new cases per year in Canada.”

- Dr. Marc de Perrot
A TRACK RECORD OF SUCCESS

The Mesothelioma Program’s strong track record for quality care, thanks to the close collaboration of surgeons, radiologists, nurses and respiratory therapists, makes the program uniquely poised to improve the efficiency of all services offered to mesothelioma patients. Some world-firsts include:

- Conducting clinical trials with radiation before surgery that can double the survival rate for patients from 32% to 72%.
- A world-unique CT-based early detection program for patients exposed to asbestos.
- The only comprehensive program in the world that provides mesothelioma patients with a one-stop resource (prevention, diagnosis, screening, therapy, etc.), often within 24 hours.

ASBESTOS AND MESOTHELIOMA

As you are aware, extended exposure to asbestos can cause grave health risks for trade workers. No matter how careful trade workers are, it’s extremely difficult for them to completely avoid asbestos, a carcinogen that infiltrates a lot of construction materials and dust, especially in older buildings.

When swallowed or inhaled over the long term, asbestos fibres act like microscopic needles that work their way into the lining of workers’ lungs and can develop into tumours. Mesothelioma typically appears 20-40 years after exposure, which is why the number of new cases of this insidious cancer is still growing, even though asbestos was banned in Canada in the early 1980s.

What makes mesothelioma so difficult to treat is that some of these fibers and cancerous cells escape during surgery, causing the cancer to spread into the other lung and abdomen. If the aggressive cancer is left untreated, it can spread to other organs. Half of all patients currently die within a year of being diagnosed. But if caught early enough, trade workers can benefit from various treatment options and better survival rates.
LIFE-CHANGING PROGRAMS NOW UNDERWAY

1) THE RAPID ASSESSMENT AND MANAGEMENT PROGRAM
THE NEED: $300,000 ANNUALLY

The Princess Margaret takes the health and needs of trade workers seriously. We believe it’s important to offer trade workers efficient services when they work long hours, potentially being exposed to harmful substances. Our first priority is to shorten the time between diagnosis and treatment. Typically, a referral to a specialized centre can take several months and support is often not available to patients and their families.

That’s why The Princess Margaret established a rapid assessment and diagnosis program that assesses patients with respiratory problems related to asbestos in one day. Currently, 70% of patients are diagnosed with mesothelioma at Stage 3, so earlier detection and swift access to treatment is crucial.

Rapid Assessment and Diagnosis Program One-Day Schedule

*The Interventional Thoracic Surgery Suite, the first of its kind in North America, is a state-of-the-art surgical suite equipped with high-end technology at Toronto General Hospital. It helps fast-track patients referred to the Mesothelioma Program by performing diagnostic and therapeutic procedures, in a minimally invasive way, as a day procedure.*
2) THE EARLY DETECTION PROGRAM: AN UNRIVALLED WORLD-CLASS INITIATIVE
THE NEED: $520,000 ANNUALLY

The Princess Margaret is the only facility in the world conducting the Early Detection of Mesothelioma and Lung Cancer in Prior Asbestos Workers using a Low-Dose Computed Tomography (LDCT) study in conjunction with the Mesothelioma Program.

Computed tomography (or CT scan) uses a large donut-shaped x-ray machine to capture images at many different angles around the body. A computer assembles those x-ray “slices” into cross-sectional or 3D images of internal organs, like the lungs.

No other program in the world has the ability to detect mesothelioma and other asbestos-related diseases at an early stage. A benefit of the Early Detection Program is that trade workers will receive important information on how to protect themselves now, before it’s too late. If an individual is diagnosed with mesothelioma, treatments are given to help slow the progress of the disease.

Which Candidates Are Involved?
The team screens individuals 30 years or older who have no symptoms and enjoy good health, but have a strong history of exposure to asbestos (at least twenty years ago) or show evidence of asbestos exposure on their X-rays in the form of lung scarring. Currently there are over 1,300 individuals in the screening program, one of the largest in the world.

How Does Early Screening Work?
At the time of CT screening, a small blood sample is drawn and used as a biomarker. Blood biomarkers help to diagnose various cancers earlier. Increased levels of proteins may indicate that a mesothelioma tumour is developing, because those levels are much higher in patients with mesothelioma. Combining biomarkers with screening CT scans can provide an even earlier detection of mesothelioma than CT scans alone. An earlier diagnosis means more effective treatment for trade workers and a chance at prolonging their life.
Clinicians and Researchers
Trade workers can rest assured that The Princess Margaret has their best mesothelioma specialists leading the Early Detection Program. The two principal investigators directing the program are Dr. Demetris Patsios and Dr. George Dong, both radiologists, who have been working in this field for over 15 years. Screening former trade workers detects advanced malignant mesothelioma, as well as early and late-stage lung cancer.

Dr. Ming-Sound Tsao, an internationally-acclaimed lung cancer pathologist, is also involved in the study and is currently investigating mesothelin-related proteins and the osteopontin protein in individuals who have a history of asbestos exposure.

In June 2012, Dr. Tsao won the prestigious O. Harold Warwick Award from the Canadian Cancer Society for Excellence in Lung Cancer Research.

The Downfall of a Costly Program
The Early Detection Program is an expensive initiative that costs The Princess Margaret approximately $520,000 annually. This amount covers costs like program coordinators’ salaries, CT equipment and maintenance, database maintenance and general supplies.

The screening alone costs $260,000 annually. With these expenses and little monetary support coming in the door, the program may have to begin limiting the number of individuals screened for mesothelioma and other asbestos-related diseases.

This news is gravely unfortunate when the focus should be on program expansion.

3) THE S.M.A.R.T. TECHNIQUE: RADIATION BEFORE SURGERY - A WORLD FIRST
THE NEED: $500,000 ANNUALLY

A revolutionary treatment developed by Dr. John Cho, a radiation oncologist, in collaboration with Dr. Marc de Perrot, can double the survival rate of mesothelioma patients at The Princess Margaret.

Instead of the usual treatment of radiation treatment after surgery, Dr. Cho suggested giving a high, precise dose of radiation before surgery. Dubbed the “S.M.A.R.T.” technique (for Surgery for Mesothelioma After Radiation Therapy), this experimental approach uses high doses of radiation over five days. Through precise targeting of the diseased area, doctors are able spare the heart, spine, and other healthy tissue. The idea is to kill cancer cells so they aren’t able to seed
themselves in the other lung or abdomen during surgery. To protect the patient from the damaging effects of high doses of radiation, surgery to remove the affected lung is performed within a week.

“The 25 patients in our four-year study experienced shorter treatment, fewer complications and speedier recovery,” said Dr. Cho. “The three-year survival rate more than doubled to 72% from 32%.”

The S.M.A.R.T. technique also reduced the treatment cycle for patients to one month from five months.

Drs. Cho and de Perrot’s success has drawn attention from around the world. Study results were published in the January 2014 issue of the Journal of Thoracic Oncology. Doctors at the Mayo Clinic in Minnesota will soon be attempting to replicate their method. Drs. Cho and de Perrot also presented their findings at the 15th World Conference on Lung Cancer in Sydney, Australia in October 2013.

“These results offer real hope to mesothelioma patients,” says Dr. de Perrot. With the S.M.A.R.T. technique still only five years into development, survival rates for mesothelioma could be improved even further in the years to come.

MAN HONG CHAN: A LIFE EXTENDED

It took more than two decades before former Ontario Hydro mechanic, Man Hong Chan, knew anything was wrong with his lungs.

Then, in his 60s, he began feeling short of breath while playing soccer. Soon after, he received a frightening diagnosis. Mr. Chan had developed mesothelioma, a rare and aggressive form of lung cancer, from exposure to asbestos on the job 20 years ago.

“It was scathing news. I was really scared,” he said. “Most people don’t even last two years.”

The Princess Margaret’s world-leading S.M.A.R.T. technique rid him of his tumour. Now 74 years old, Mr. Chan has been cancer free for more than four years.
4) TRIMODALITY THERAPY FOR MESOTHELIOMA PATIENTS: 
THE BENEFITS OF SURGERY ALONGSIDE RADIATION AND CLINICAL CARE

Every trade worker diagnosed with mesothelioma at The Princess Margaret undergoes a thorough investigation and is offered the treatment that is most appropriate for their condition. Depending on how far their mesothelioma has progressed, and their general health, this may vary from an aggressive treatment designed to cure their cancer, to a course of therapy aimed at controlling symptoms and making the person comfortable.

Currently, the only recognized standard of care for malignant mesothelioma is the drug Cisplatin, combined with an antifolate agent that stops the production of folic acid, which can interfere with some kinds of chemotherapy.

This combination does improve median survival rates for patients, but the number of extra months of life the patient receives (typically from 9 to 12 months) is discouraging - even in the best group of patients.

In response, Dr. de Perrot developed a “trimodality” therapy that combines chemotherapy, surgery and radiation for patients with early stage mesothelioma. He’s so optimistic that survival rates will improve with this approach that he presented his promising findings to hundreds of cancer specialists last August at the 8th Annual Ontario Thoracic Cancer Conference.

Additionally, current research in the mesothelioma program’s lab suggests that the positive effects of trimodality therapy could potentially be strengthened with the use of drugs to boost the immune system during radiation or after radiation.

The team encourages mesothelioma patients to participate in clinical trials for their own potential benefit and to help doctors and researchers at The Princess Margaret to continue improving treatment options for all patients, now and in the future.
5) USING THE IMMUNE SYSTEM TO FIGHT MESOTHELIOMA  
THE NEED: $1,000,000 ANNUALLY

Dr. de Perrot is collaborating with Dr. Pamela Ohashi, a Senior Scientist at The Princess Margaret and a world leader in an exciting and innovative approach that uses the body’s own immune system to fight mesothelioma. This strategy involves removing the patient’s white blood cells, “super charging” them outside of the body for four to six weeks, and then implanting them back into the patient to fight their cancer. Recent tests have shown that 50% of patients with melanoma have responded positively to this approach, and tests for mesothelioma patients began in January 2014. Less toxic than traditional cancer treatments, immune therapy is especially effective for older patients who may not be strong enough for surgery. For trade workers with mesothelioma, immune therapy is a more natural therapy that provides a better quality of life during treatment.

6) CHEMO-IMMUNOTHERAPY: IMPROVING PATIENT OUTCOME  
THE NEED: $480,000 ANNUALLY

Princess Margaret researchers are also figuring out how to use the body’s own immune system to boost the effectiveness of chemotherapy against mesothelioma. Dr. Licun Wu and his team are focusing on the behavior of the immune system between cycles of chemotherapy.

“Cancer cells tend to repopulate during breaks between chemotherapy treatments. Evidence has shown that the rate of repopulation of surviving cancer cells accelerates over time, so better approaches to stop this process must be developed.” - Dr. Wu.

Dr. Wu has found that blocking the actions of CTLA-4, a protein that acts as a brake on certain immune responses, helps prevent mesothelioma cells from repopulating during breaks in chemotherapy. Reining in on this protein may allow a type of immune cell known as a natural killer T-cell to flourish and fight the disease.

This study lays the groundwork for clinical trials that use drugs that can block CTLA-4. Diversifying the types of treatments available will give trade workers more than one way to fight mesothelioma!
7) CLINICAL TRIALS TO IMPROVE DISEASE STABILITY AND IMPROVE PATIENTS’ QUALITY OF LIFE

a) Phase II Study of the Drug Tremelimumab for Patients with Inoperable Mesothelioma

Tremelimumab is a manufactured antibody similar to ones that are made by the human body to fight off infection. This antibody blocks cytotoxic T-lymphocyte antigen 4 (CTLA4), a protein that can put a brake on certain immune responses. This experimental drug was developed to stimulate the immune system as a new way of killing cancer cells. A clinical trial, led by Dr. Ron Feld, a medical oncologist at The Princess Margaret, may lead to a second line of treatment for mesothelioma patients that will improve their quality of life.

b) Phase II Study of the Drug VS-6063 for Patients with Advanced Mesothelioma

VS-6063 is a drug that is designed to inhibit a mutation called FAK, creating a loss in a tumour marker called Merlin. Initial studies have shown that there seems to be a survival benefit for patients with advanced mesothelioma who have lost that tumor marker.

This double-blind, placebo controlled, multicenter study involves patients with malignant pleural mesothelioma who have not progressed. That means their tumours have either stayed the same or only had partial shrinkage after four cycles of chemotherapy, called “first line” treatment. Our researchers are urgently trying to find new options for mesothelioma patients who are not responding to first line treatment. Because no more than four to six cycles of platinum-based chemotherapy are generally recommended for patients with advanced disease, non-progressing patients enter a “watch and wait” period with periodic review until progression. Currently there are no approved therapies following first line treatment for mesothelioma. Limited results from the Phase I trials suggests that Merlin loss in recurrent mesothelioma may stop the cancer from growing.

8) BLOOD TEST FOR MONITORING MESOTHELIOMA

Researchers are investigating the possibility that a simple blood test could be used to help diagnose and monitor various cancers. As a tumour develops, it sheds certain proteins that can be detected in the blood. Some protein levels are much higher in patients with mesothelioma, compared to healthy people who have had asbestos exposure. Increased levels of proteins in healthy subjects may predict that a mesothelioma tumour is developing or recurring. This non-invasive and cost-effective strategy involves drawing a small blood sample at the time of CT screening and looking for the proteins that could indicate cancer. Combining these tumour markers with CT scans may provide an even earlier detection of mesothelioma than CT scans alone.
MESOTHELIOMA RESEARCH PROGRAM UPDATE

Support for the Mesothelioma Research Program is generously provided by:

Asbestos Workers Local 110
Building and Construction Trades Council of Ontario
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International Brotherhood of Boilermakers Local 128
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Pinchin Environmental Ltd
Provincial Building & Construction Trades Council of Ontario
Sarnia Occupational Health Clinic for Ontario Workers
United Association of Journeymen & Apprentices Local 67
United Association of Plumbing and Pipe Fitting Local 46

A special thank you to all those donors honouring loved ones through their support.
THANK YOU

The hundreds of Canadians each year who are diagnosed with mesothelioma still have too few treatment options open to them. That's why the support of partners like you is so crucial to offering new hope to our patients and their families.

Recent developments at The Princess Margaret have demonstrated that a mesothelioma diagnosis does not have to mean a death sentence. Your donations have enabled the development of pioneering approaches that are transforming and extending lives of people with mesothelioma. Your commitment has also funded the training of thoracic surgeons, radiologists, clinicians and researchers that will lead the search for new treatments in the future.

Together, we are having a profound impact on the fight against mesothelioma, here at The Princess Margaret, and around the world.

Thank you for recognizing the crucial need for continued research to find new treatments in mesothelioma. On behalf of all the trade workers and other patients who are benefitting from your generosity, thank you for your help with this life-changing work!
**HOW TO PARTICIPATE IN THE MESOTHELIOMA RESEARCH PROGRAM**

**The Early Detection Project** continues to actively recruit individuals from high risk occupations. In order to qualify for the study, individuals must have been exposed to asbestos at least 20 years ago, and/or have pleural plaques on chest x-rays, be 30 years of age or older and in general good health with no history of prior cancers.

For further information, or to schedule an appointment, contact: 416-340-5686 or brenda.osullivan@uhn.on.ca.

**The Rapid Assessment and Management Program** is now handling more than double the number of referred patients with asbestos-related lung diseases than it was two years ago. The clinic continues to accept new patients.

For further information on this program, please call 416-340-5686 or a referral can be faxed to 416-340-4964.

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